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Midlife cardiovascular status and old age physical functioning trajectories
in older business men

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40 ABSTRACT

41 Background. The associations between cardiovascular disease (CVD) risk and later physical
42 functioning have been observed, but few studies with follow-up into old age exist. We
43 investigated the association between cardiovascular status in midlife and physical functioning
44 trajectories in old age.

45 Methods. In the Helsinki Businessmen Study cohort (Caucasian men born in 1919-1934) three
46 CVD status groups were formed based on clinical measurements carried out in 1974: signs of
47 CVD (diagnosed clinically or with changes in ECG, chronic disease present or used medication,
48 $n=563$); healthy and low CVD risk ($n=593$) and high CVD risk ($n=1222$). Of them, 1560 men had
49 data on physical functioning from at least one of four data collection waves between 2000-
50 2010. Ten questions from the RAND-36 (SF-36) survey were used to construct physical
51 functioning trajectories with latent class growth mixture models. Mortality was accounted for
52 in competing risk models.

53 Results. A five-class solution provided the optimal number of trajectories: 'intact', 'high stable',
54 'high and declining', 'intermediate and declining' and 'consistently low' functioning. Compared
55 to low CVD risk, high CVD risk in midlife decreased the risk of being classified into the 'intact'
56 (fully adjusted $\beta -3.98$, SE 2.0, $p=0.046$) relative to 'consistently low' physical functioning
57 trajectory. Compared to low CVD risk, those with signs of CVD were less likely to follow the
58 'intact', 'high stable' or 'high and declining' relative to the 'consistently low' trajectory (all
59 $p<0.018$).

60 Conclusions. Among businessmen, a more favorable CVD profile in midlife was associated with
61 better development of physical functioning in old age.

62 Key words: Cardiovascular health, physical functioning trajectories, growth mixture model,
63 life course epidemiology, healthy ageing

INTRODUCTION

Adequate physical functioning is important in maintaining independence and quality of life with advancing age.¹ Associations between poor physical functioning and adverse outcomes such as geriatric syndromes, nursing home admission and premature mortality²⁻⁶ stress the importance of identifying modifiable risk factors in time. Knowledge on these risk factors may help in designing interventions aimed at maintaining the ability to actively engage in society and live independently.⁷

Evidence from longitudinal studies suggests that individual modifiable cardiovascular risk factors such as high blood pressure and cholesterol, smoking, obesity and hyperglycemia are linked with later physical functioning.⁸⁻¹² While the association of clusters of three or four CVD risk factors¹³⁻¹⁵ and established composite CVD risk indices¹⁶⁻¹⁹ and later physical functioning measures have been studied, only few studies with follow-up from midlife into old age exist.^{15,16,18,19} Furthermore, little is known about whether and how midlife cardiovascular status is associated with various trajectories of physical functioning in old age. There is marked heterogeneity in the progression of physical functioning with advancing age²⁰ and it is influenced by current, but also past risk factors. More information on early risk factors for patterns of physical functioning in older age would provide insight into more targeted promotion of functioning. We investigated the association between modifiable midlife cardiovascular risk factors measured in the year 1974 and physical functioning trajectories in old age, which had been assessed at four time points over a 10-year period between 2000 and 2010.

MATERIALS AND METHODS

Study population

The Helsinki Businessmen Study (HBS) cohort has been described in detail earlier.²¹ Briefly, the present study population consisted of white men born between 1919 and 1934. They shared a similar working status and belonged to the highest socioeconomic class. Between the years 1964 and 1973, 3490 men participated in voluntary health check-ups at the Finnish Institute of Occupational Health that included measurements on CVD risk factors which were considered to be important at that time. Of these men, 3309 formed the baseline cohort for later examinations, see Figure 1. During the years 1972-73 these men were screened for eligibility for a CVD primary prevention trial and in 1974, 1222 men were assessed as having high or low CVD risk or signs of CVD (see below for definitions of CVD risk).²¹ During 1974-1980, 1222 high CVD risk men participated in a multifactorial prevention trial,²² but participation in the trial did not affect the present analyses and all men were included to improve statistical power. Of the 2378 men who had data on CVD status in 1974, 1560 had data on physical functioning from at least one of the four subsequent data collection waves carried out in the years 2000, 2003, 2007 and 2010 (response rates were 81.5%, 66.3%, 65.1%, 67.8%, respectively) and they formed the analytical sample of this study. The follow-up studies of the HBS have been approved by the Ethics Committee of the Department of Medicine, Helsinki University Hospital, Finland and the study has been registered as Clinical Trials.gov identifier: NCT02526082.

Cardiovascular status and risk definitions in midlife

Examinations for CVD risk factors and health status were carried out in 1974 at a mean age of 47.3 (SD 4.0) years. Overweight was determined by relative body weight (%) (body weight in kilograms x 100 divided by height in centimeters minus 105).²³ Smoking was inquired in a

questionnaire asking how many cigarettes per day they smoked. Blood pressure was measured in a sitting position after 10 min rest using a mercury sphygmomanometer. Fasting serum cholesterol and triglycerides were measured using standard methods. Blood glucose (mmol/L) was measured 1 hour after a glucose load of 1g/kg of body weight administered orally. Resting and exercise electrocardiograms were taken at the laboratory and medical history was recorded. In 1974, cohort members were classified into groups according to risk factors and possible signs of CVD and other chronic diseases.²² The CVD risk factors and cut-offs were defined as follows: 1) relative body weight $\geq 120\%$ (corresponds to BMI ≥ 27.8 kg/m²); 2) smoking >10 cigarettes/day; 3) blood pressure $\geq 160/95$ mmHg; 4) serum cholesterol ≥ 7.0 mmol/L (corresponds to 6.4 mmol/L with current laboratory methods); 5) serum triglycerides ≥ 1.7 mmol/L; and 6) 1-hour post-load glucose ≥ 9.0 mmol/L.²² The distribution of risk factors in our analytical sample (according to cut-offs described above) was as follows: 41.4% had one, 32.2% had two, 17.0% had three and 9.4% four or more CVD risk factors. It is of note that risk definitions reflected the situation in the 1970's. Albeit according to current standards, low-risk men would rather be defined to be at "intermediate" risk, we wanted to use the original CVD grouping that has been reported in several papers.^{22,24}

Three CVD status groups were formed: 1) low CVD risk (n=593, healthy, no signs of CVD, none of the aforementioned risk factors); 2) high CVD risk (n=1222, healthy, no signs of CVD, but had at least one of the CVD risk factors, mean 2.1 risk factors); and 3) signs of CVD (n=563, CVD diagnosed either clinically or with changes in ECG, receiving regular medication for hypertension, hyperlipidemia or diabetes, or having been diagnosed with serious non-CVD). The last group was named 'signs of CVD' while the majority of the conditions that the men had were cardiovascular diseases or related to the metabolic system.

136

137 Physical functioning

138 In the year 2000 at a mean age of 73.3 (SD 4.1) years, physical functioning was assessed using
 139 ten items included in the physical functioning domain from the validated RAND-36 Health
 140 Survey (Version 1.0) (identical with the Short Form SF-36).^{25,26} Cohort members were asked to
 141 what extent their health limited daily activities such as walking two or half a kilometer or 100
 142 meters or climbing 1 or several flight of stairs. If the participants had no difficulties, some
 143 difficulties or they were unable to perform a task, these were coded as 100, 50 and 0,
 144 respectively, they were summed up and divided by 10. Scores range from 0 to 100 and a higher
 145 score indicated better physical functioning. For each data collection wave, 7 out of the 10
 146 physical functioning items were required for the score to be calculated (and in that case the
 147 summed score was divided by the respective number of answered items). The proportion of
 148 those who had data missing on three items at most ranged between 1.0 and 1.7% across the
 149 four data collection waves and when considering all four follow-ups the percentage of those
 150 with 7 out of 10 answers for each follow-up we were able to include 48 persons (3.1%).

151

152 Health characteristics in midlife and old age

153 The cohort members were inquired in 1974 about self-rated health with response alternatives:
 154 very good, fairly good, average, fairly poor and very poor. For the analyses, two latter ones were
 155 coded into one category "poor" due to few cases in the very poor category.²⁷ In the year 2000,
 156 the participants were asked about physician-diagnosed illnesses in a mailed questionnaire. The
 157 men who reported having at least one of the following diseases: stroke, transient ischemic
 158 attack, high blood pressure, coronary artery disease, heart failure, or dysfunction in
 159 cerebrovascular or lower extremity circulation were classified as having CVD. Dates of death

were retrieved from the Finnish Population Register Center for the entire cohort between 1974 and 2010.

Statistical methods

We identified different physical functioning trajectories by fitting latent class growth mixture models (LGMM) to all available physical functioning data of the 1560 cohort members from the years 2000, 2003, 2007 and 2010 using Mplus version 7.0.²⁸ In the analyses, we used LGMM with Full Information Maximum Likelihood, in order to capture unobserved subpopulations (latent groups) in all available data with similar physical functioning trajectories, but which were distinct across the latent groups over the follow-up time. Grouping was based on the likelihood of the membership calculated for each individual's own trajectory. Each latent group had their own growth parameters, intercept (indicating similar trajectories over time) and slope (indicating changes in physical functioning scores over time). We estimated the quadratic and cubic shapes of the trajectories in order to identify all potential differences in the development of physical functioning. We used several model fit indices to determine the optimal number of latent groups.²⁸ For Bayesian Information Criterion (BIC) and Akaike Information Criterion (AIC), lower values indicate a better fit of the model. Clarity of classification into trajectory classes was assessed with 1) high percentage of individuals falling into the latent class based on the posterior probabilities (indicates the probability of a participant belonging in a given trajectory class) and 2) high model entropy (an aggregate of posterior probabilities), which ranges between 0 and 1, with values near 1 indicating clear classification.

The conceptual model for investigating the association between CVD status in midlife and physical functioning trajectories in old age is presented in Figure 2. We constructed a competing

risks multinomial regression model to model the risk related to physical functioning trajectory class membership while simultaneously accounting for mortality risk during the physical functioning assessments between the years 2000 and 2010. Kaplan-Meier survival curves did not cross for the major part of time thus supporting proportionality. The proportionality of hazards was tested using the scaled Schoenfeld residuals, where non-significant p-values lend support for the proportionality assumption. The proportionality was supported for all covariates with an effect in the mortality part of the model: CVD status in y. 1974 (high risk vs. rest, $p=0.575$; sick vs. rest, $p = 0.797$), self-rated health in y. 1974 ($p=0.629$), CVD in y. 2000 ($p=0.669$) and the global estimate of proportionality ($p=0.875$). We estimated unstandardized regression coefficients (β), their mean errors (SE) and related p-values for the associations. Based on the proportional hazards model, the latent effect of excess mortality risk was used to adjust the physical functioning trajectory class for mortality risk. In addition, the model was adjusted for birth year, self-rated health in midlife and self-reported CVD in the year 2000. 71 (4.6%) individuals had missing data for self-rated health, which were imputed using multiple imputation in SPSS with data on all intact variables included in the prediction of missing values. Significance level was set at 0.05 and tests were two sided.

RESULTS

The model fit indices used to determine the best model fit for the physical functioning data in the 10-year follow-up indicating the optimal number of latent classes, i.e. physical functioning trajectories, are presented in the Supplementary Table S1. BIC was lowest for the five-class solution. Average membership probabilities in the five latent classes ranged between 0.78 and 0.88, while model entropy was 0.71 indicating reasonable classification clarity. The five physical functioning trajectories were named 'intact' (approximately 10% of the cohort belonged to this

class), 'high stable' (32%), 'high and declining' (29%), 'intermediate and declining' (23%), and 'consistently low' (6%) (Figure 3). Individual observations belonging to each physical functioning trajectory are presented in Supplementary Figure S1.

There were statistically significant differences in the characteristics of the cohort members across the physical functioning trajectories presented in Table 1. The men classified into the 'intact' and 'high stable' trajectory were younger at baseline, 45.2 (SD 3.6) and 46.5 (SD 3.9) years, respectively, whereas those in the 'consistently low' trajectory were the oldest 49.0 (3.8) years. The proportion of men with signs of CVD was higher in the poorer physical functioning trajectories (7.7% in the 'intact' vs. 33.7% in the 'consistently low' trajectory). There were also differences for self-rated health in midlife across the trajectories; of those in the 'intact' trajectory, 44.0% rated their health very good or fairly good, whereas the corresponding proportion was 19.0% in the 'consistently low' trajectory. The prevalence of CVD in the year 2000 was 31.0% for the men assigned to the 'intact' trajectory and increased in the poorer physical functioning trajectories being 85.4% in men belonging to the 'consistently low' trajectory. Out of the 1560 cohort members, 539 (34.6%) died between the years 2000 and 2010. Mortality during ten years was higher among those who were classified into the poorer physical functioning trajectories (17.6% in the 'intact' trajectory vs. 84.3% in the 'consistently low' trajectory).

The results of the associations between midlife CVD status and physical functioning trajectories in old age for the competing risk multinomial regression models are presented in Table 2. Compared to those with low CVD risk in midlife, those with high CVD risk were less likely to be

classified into the 'intact' (fully adjusted β -3.98, SE 2.0, $p=0.046$) trajectory relative to 'consistently low' physical functioning trajectory. In terms of effect size, the associations were parallel for the 'high stable' and 'high and declining' trajectories but not statistically significant. Compared to the men with low CVD risk, those with signs of CVD in midlife were also less likely to be classified into the 'intact', 'high stable' and 'high and declining' physical functioning trajectory relative to the 'consistently low' trajectory, all p -values <0.018 . The association was also parallel but statistically non-significant for the 'intermediate and declining' trajectory. The proportion of those who died during the follow-up increased gradually with declining physical functioning trajectories. The prevalence of mortality was lowest among those in the 'intact' trajectory (approximately 18%) and highest among those in the 'intermediate and declining' (54%) and 'consistently low' trajectories (84%), p -value <0.001 .

DISCUSSION

We identified five distinct physical functioning trajectories during a 10-year period in a cohort of old business executives who have been followed up from midlife. Albeit around forty percent of the men were classified into the 'intact' or 'high stable' physical functioning trajectory, a fair number of cohort members showed signs of declining physical functioning which progressed during the follow-up period in old age. A clinically significant decrease of 5 or more points²⁹ in the RAND-36 physical functioning sub-category score was observed in all other trajectories except for the 'intact' trajectory. A more favorable CVD profile in midlife was associated with better development of physical functioning in old age. Compared to low CVD risk, those with high CVD risk or signs of CVD were less likely to follow one of the four more favorable physical functioning trajectories. The association persisted after adjustment for CVD in old age and also after accounting for mortality as a competing risk. Our findings provide new evidence on the

long-term association between modifiable CVD risk factors and subsequent patterns of physical functioning.

Previous studies have found that higher CVD risk scores, indicating impaired cardiovascular health, are related to poorer subsequent physical functioning.¹⁶⁻¹⁹ However, to the best of our knowledge, there are no previous studies on the patterns of physical functioning that are related to earlier CVD status. In the present study, high CVD risk in midlife decreased the probability of being assigned to a physical functioning trajectory that was intact across the 10-year follow-up of physical functioning in old age. For the men with signs of CVD in midlife, i.e. CVD diagnosed either clinically or with changes in ECG, receiving regular medication for hypertension, hyperlipidemia or diabetes, or having been diagnosed with serious non-CVD, the association was more pronounced. Signs of CVD decreased the probability of being assigned to a more favorable physical functioning trajectory in old age. This association was observed for those men who were assigned to the 'consistently low', 'high and declining' and 'high stable' functioning trajectories compared to those in the 'intact' trajectory. This might be due to disease-related impairments and decreased level of reserve capacity and compensation ability in midlife which may have later led to functional decline.³⁰

The mechanisms underlying impaired physical functioning are complex and may include many physiological changes related to disease processes and geriatric syndromes.^{6,31} For example, smoking and hypertension may lead to peripheral artery disease which predisposes to declining physical functioning.³² Furthermore, damage to the musculoskeletal and peripheral nervous systems start to occur well before the consequences for physical functioning can be detected. Evidence that the onset of the chronic disease burden starts already early on in life is growing.³³

Notably, early detection of risk factors that are known to subsequently be related to disability later in life help to identify individuals who potentially stand to gain from preventive health care measures.³⁰ Modelling physical functioning trajectories provide more knowledge on the progress of limitation and the timing of preventive measures for maintaining physical capability.

The strengths of our study include the well-characterized sample of businessmen and executives who came from a homogenous background and who have been followed up across several decades. Midlife cardiovascular status was determined based on measurement/assessment of several CVD risk factors which is similar to other established CVD risk scores such as the Framingham Risk Score.³⁴ Physical functioning was assessed using the ten items included in the sub-scale of physical functioning from the validated RAND-36 Health Survey questionnaire²⁵ and having several data collection waves allowed for modeling trajectories over time. GMM analyses are data-driven and a person-centered approach to classifying study participants into sub-groups in a post-hoc manner. The method can be used to describe differences in longitudinal change between and within the unobserved groups. We used a competing risk model to account for mortality that occurred during the 10-year physical functioning follow-up among the old businessmen.

Some limitations of the study should be recognized. The cohort comprised of men only and included individuals belonging to the highest socioeconomic strata which limits generalizability. The business executives and managers at that time worked typically long hours and the work was often stressful. These aspects of work have been shown to contribute to a higher prevalence of CVD.³⁵ We did not have the same measures of CVD risk available in old age that we had in midlife and were not able to investigate the long-term association between CVD risk

status and later outcomes. During the follow-up of physical functioning between the years 2000 and 2010, mortality was relatively high. Using a maximum likelihood method in the GMM analyses, which uses all existing information and does not require complete data, we accounted for non-random missingness related to mortality. We also further accounted for mortality during the follow-up by using a competing risk model in the multinomial regression analyses. We did not have data on physical functioning in midlife and thus adjusted for self-rated health, which is a good general measure of health and is related to adverse outcomes in later life such as frailty.³⁶

In conclusion, in a cohort of older businessmen and executives, midlife cardiovascular status was related to physical functioning patterns in old age which varied greatly among the men. Trajectories that indicate stability/maintenance of physical functioning into old age are markers for healthy ageing and quality of life and important outcomes in terms of the individual's ability to lead an independent and active life. Our results indicate that CVD risk status in midlife is a useful measure in determining the risk of poor physical functioning decades later. Furthermore, intervening in these modifiable risk factors already in midlife might help mitigate decline in physical functioning in older age.

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Conflict of Interest

The authors declare no conflicts of interest.

329 Author contributions

330 MBvB drafted the paper, analyzed the data, designed the study; MJH interpreted the data,
331 designed the study, revised the paper critically for important intellectual content; TT
332 interpreted the data, designed the study, revised the paper critically for important intellectual
333 content; KP interpreted the data, designed the study, revised the paper critically for important
334 intellectual content; SS interpreted the data, designed the study, revised the paper critically
335 for important intellectual content; TS responsible for data acquisition, interpreted the data,
336 designed the study, revised the paper critically for important intellectual content.

337

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346 LEGENDS

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348 Figure 1 Study flowchart.

349

350 Figure 2 Conceptual model for assessment of midlife CVD status and physical functioning
351 trajectories in old age when accounting for birth year, self-rated health in midlife, CVD in older
352 age and excess mortality risk. Squares are observed values and circles are latent values.

353

354 Figure 3 Identified physical functioning trajectories over the 10-year follow-up from the year
355 2000 to 2010.

356

357 Supplementary Figure S1 Individual observations belonging to each physical functioning
358 trajectory.

359

360 Supplementary Table S1. Model Fit Statistics, Group Sizes and Average Latent Class
361 Probabilities for Most Likely Class Membership.

362

363

364 REFERENCES

- 365 1. United Nations, Department of Economic and Social Affairs, Population Division. World population
366 prospects: The 2015 revision, key findings and advance tables. Working paper no. ESA/P/WP.241. New
367 York, US: United Nations; 2015.
- 368 2. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower
369 extremity function: Association with self-reported disability and prediction of mortality and nursing
370 home admission. *J Gerontol* 1994;49:85-94.
- 371 3. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons
372 over the age of 70 years as a predictor of subsequent disability. *N Engl J Med* 1995;332:556-561.
- 373 4. von Bonsdorff M, Rantanen T, Laukkanen P, Suutama T, Heikkinen E. Mobility limitations and
374 cognitive deficits as predictors of institutionalization among community-dwelling older people.
375 *Gerontology* 2006;52:359-365.
- 376 5. Cesari M, Onder G, Zamboni V, et al. Physical function and self-rated health status as predictors of
377 mortality: Results from longitudinal analysis in the iI SIRENTE study. *BMC Geriatr* 2008;8:34-2318-8-34.
- 378 6. Rosso AL, Eaton CB, Wallace R, et al. Combined impact of geriatric syndromes and cardiometabolic
379 diseases on measures of functional impairment. *J Gerontol A Biol Sci Med Sci* 2011;66:349-354.
- 380 7. WHO. Active ageing. A policy Framework.
381 http://whqlibdoc.who.int/hq/2002/who_nmh_nph_02.8.pdf; 2002.
- 382 8. Chang M, Saczynski JS, Snaedal J, et al. Midlife physical activity preserves lower extremity function in
383 older adults: Age Gene/environment Susceptibility-Reykjavik Study. *J Am Geriatr Soc* 2013;61:237-242.
- 384 9. Strand BH, Mishra G, Kuh D, Guralnik JM, Patel KV. Smoking history and physical performance in
385 midlife: Results from the British 1946 birth cohort. *J Gerontol A Biol Sci Med Sci* 2011;66:142-149.

- 386 10. Gopinath B, Russell J, Flood VM, Burlutsky G, Mitchell P. Adherence to dietary guidelines positively
387 affects quality of life and functional status of older adults. *J Acad Nutr Diet* 2014;114:220-229.
- 388 11. Rosano C, Longstreth WT, Jr, Boudreau R, et al. High blood pressure accelerates gait slowing in well-
389 functioning older adults over 18-years of follow-up. *J Am Geriatr Soc* 2011;59:390-397.
- 390 12. Stenholm S, Sainio P, Rantanen T, et al. High body mass index and physical impairments as
391 predictors of walking limitation 22 years later in adult Finns. *J Gerontol A Biol Sci Med Sci* 2007;62:859-
392 865.
- 393 13. Chakravarty EF, Hubert HB, Krishnan E, Bruce BB, Lingala VB, Fries JF. Lifestyle risk factors predict
394 disability and death in healthy aging adults. *Am J Med* 2012;125:190-197.
- 395 14. Koster A, Penninx BW, Newman AB, et al. Lifestyle factors and incident mobility limitation in obese
396 and non-obese older adults. *Obesity (Silver Spring)* 2007;15:3122-3132.
- 397 15. Sabia S, Elbaz A, Rouveau N, Brunner EJ, Kivimäki M, Singh-Manoux A. Cumulative associations
398 between midlife health behaviors and physical functioning in early old age: A 17-year prospective
399 cohort study. *J Am Geriatr Soc* 2014;62:1860-1868.
- 400 16. Elbaz A, Shipley MJ, Nabi H, Brunner EJ, Kivimäki M, Singh-Manoux A. Trajectories of the
401 Framingham general cardiovascular risk profile in midlife and poor motor function later in life: The
402 Whitehall II Study. *Int J Cardiol* 2014;172:96-102.
- 403 17. Jin Y, Tanaka T, Ma Y, Bandinelli S, Ferrucci L, Talleawkar SA. Cardiovascular health is associated
404 with physical function among older community dwelling men and women. *J Gerontol A Biol Sci Med*
405 *Sci.* 2017;72:1710-1716.
- 406 18. Windham BG, Harrison KL, Lirette ST, et al. Relationship between midlife cardiovascular health and
407 late-life physical performance: The ARIC study. *J Am Geriatr Soc* 2017;65:1012-1018.

- 408 19. Dhamoon MS, Dong C, Elkind MS, Sacco RL. Ideal cardiovascular health predicts functional status
 409 independently of vascular events: The Northern Manhattan Study. *J Am Heart Assoc*
 410 2015;4:10.1161/JAHA.114.001322.
- 411 20. Hardy SE, Dubin JA, Holford TR, Gill TM. Transitions between states of disability and independence
 412 among older persons. *Am J Epidemiol* 2005;161:575-584.
- 413 21. Strandberg TE, Salomaa V, Strandberg AY, et al. Cohort profile: The Helsinki Businessmen Study
 414 (HBS). *Int J Epidemiol* 2016;45:1074.
- 415 22. Miettinen TA, Huttunen JK, Naukkarinen V, et al. Multifactorial primary prevention of
 416 cardiovascular diseases in middle-aged men. Risk factor changes, incidence, and mortality. *JAMA*
 417 1985;254:2097-2102.
- 418 23. Gray D & Fujioa K. Use of relative weight and body mass index for the determination of adiposity. *J*
 419 *Clin Epidemiol*. 1991;44:545-50
- 420 24. Strandberg TE, Salomaa VV, Naukkarinen VA, Vanhanen HT, Sarna SJ, Miettinen TA. Long-term
 421 mortality after 5-year multifactorial primary prevention of cardiovascular diseases in middle-aged
 422 men. *JAMA* 1991;266:1225-1229.
- 423 25. Aalto AM, Aro S, Aro AR, Mähönen M. RAND 36-item Health Survey 1.0. Finnish version on the
 424 health-related quality of life questionnaire. Helsinki, Finland: Stakes; 1995.
- 425 26. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-item Health Survey 1.0. *Health Econ* 1993;2:217-
 426 227.
- 427 27. Huohvanainen E, Strandberg AY, Stenholm S, Pitkälä KH, Tilvis RS, Strandberg TE. Association of
 428 self-rated health in midlife with mortality and old age frailty: A 26-year follow-up of initially healthy
 429 men. *J Gerontol A Biol Sci Med Sci* 2016;71:923-928.

- 430 28. Muthen,L.K,Muthen,B.O. Mplus user's guide. Los Angels, CA: Muthen & Muthen; 1998.
- 431 29. Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences
432 of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-
433 36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities.
434 Arthritis Rheum 2001;45:384-91.
- 435 30. Ferrucci L, Cooper R, Shardell M, Simonsick EM, Schrack JA, Kuh D. Age-related change in mobility:
436 Perspectives from life course epidemiology and geroscience. J Gerontol A Biol Sci Med Sci
437 2016;71:1184-1194.
- 438 31. Strandberg TE, Pitkälä KH, Tilvis RS, O'Neill D, Erkinjuntti TJ. Geriatric syndromes-vascular
439 disorders? Ann Med 2013;45:265-273.
- 440 32. McDermott MM, Liu K, Greenland P, et al. Functional decline in peripheral arterial disease:
441 Associations with the ankle brachial index and leg symptoms. JAMA 2004;292:453-461.
- 442 33. Belsky DW, Caspi A, Houts R, et al. Quantification of biological aging in young adults. Proc Natl Acad
443 Sci U S A 2015;112:E4104-110.
- 444 34. D'Agostino RB S, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary
445 care: The Framingham Heart Study. Circulation 2008;117:743-753.
- 446 35. Nyberg ST, Fransson EI, Heikkilä K, et al. Job strain and cardiovascular disease risk factors: Meta-
447 analysis of individual-participant data from 47,000 men and women. PLoS One 2013;8:e67323.
- 448 36. Stenholm S, Kivimäki M, Jylhä M, et al. Trajectories of self-rated health in the last 15 years of life by
449 cause of death. Eur J Epidemiol 2016;31:177-185.

Table 1 Characteristics of the Cohort Members According to Physical Functioning Trajectories

	Physical functioning trajectories*					p-value
	Intact n=142	High stable n=518	High and declining n=440	Intermediate and declining n=371	Consistently low n=89	
Birth year, %						<0.001
1919-1925	20.4	31.1	40.2	54.2	53.9	
1926-1933	79.6	68.9	59.8	45.8	46.1	
Age in 1974, years, mean (SD)	45.1 (3.6)	46.5 (3.9)	47.6 (3.9)	48.5 (3.8)	49.0 (3.8)	<0.001
CVD status in 1974, %						<0.001
Low risk	43.0	33.6	32.7	18.6	13.5	
High risk	49.3	51.5	51.1	57.1	52.8	
Signs of CVD	7.7	14.9	16.2	24.3	33.7	
Self-rated health in 1974, %						<0.001
Very good	13.9	3.9	3.8	1.7	0.0	
Fairly good	40.1	35.1	32.9	22.7	19.0	
Average	40.9	50.8	52.6	54.3	51.2	
Poor	5.1	10.2	10.7	21.3	29.8	
CVD* in year 2000, %	31.0	52.1	62.7	69.0	85.4	<0.001
Died between 2000 and 2010, %	17.6	21.4	28.9	54.2	84.3	<0.001

SD= standard deviation

* Assessed between 2000 and 2010

†CVD included self-reported prevalence of stroke, transient ischemic attack, high blood pressure, coronary artery disease, heart failure, or dysfunction in cerebrovascular or lower extremity circulation.

Table 2 Unstandardized Betas, Standard Errors and P-values for Path Coefficients of Models for Midlife CVD Status Predicting Physical Functioning Trajectories in Old Age in the Helsinki Businessmen Study

	Intact vs. Consistently low			High stable vs. Consistently low			High and declining vs. Consistently low			Intermediate and declining vs. Consistently low		
	β	S.E.	p-value	β	S.E.	p-value	β	S.E.	p-value	β	S.E.	p-value
CVD status in midlife*												
Low CVD risk	ref.			ref.			ref.			ref.		
High CVD risk	-3.981	1.991	0.046	-3.768	1.984	0.058	-3.697	1.968	0.060	-2.311	1.841	0.209
Signs of CVD	-6.291	2.425	0.009	-5.752	2.402	0.017	-5.634	2.375	0.018	-3.812	2.198	0.083

CVD=cardiovascular disease

*Estimated with adjustment for birth year, self-rated health in midlife, CVD status in the year 2000 and excess mortality risk between 2000 and 2010.

Figure 1

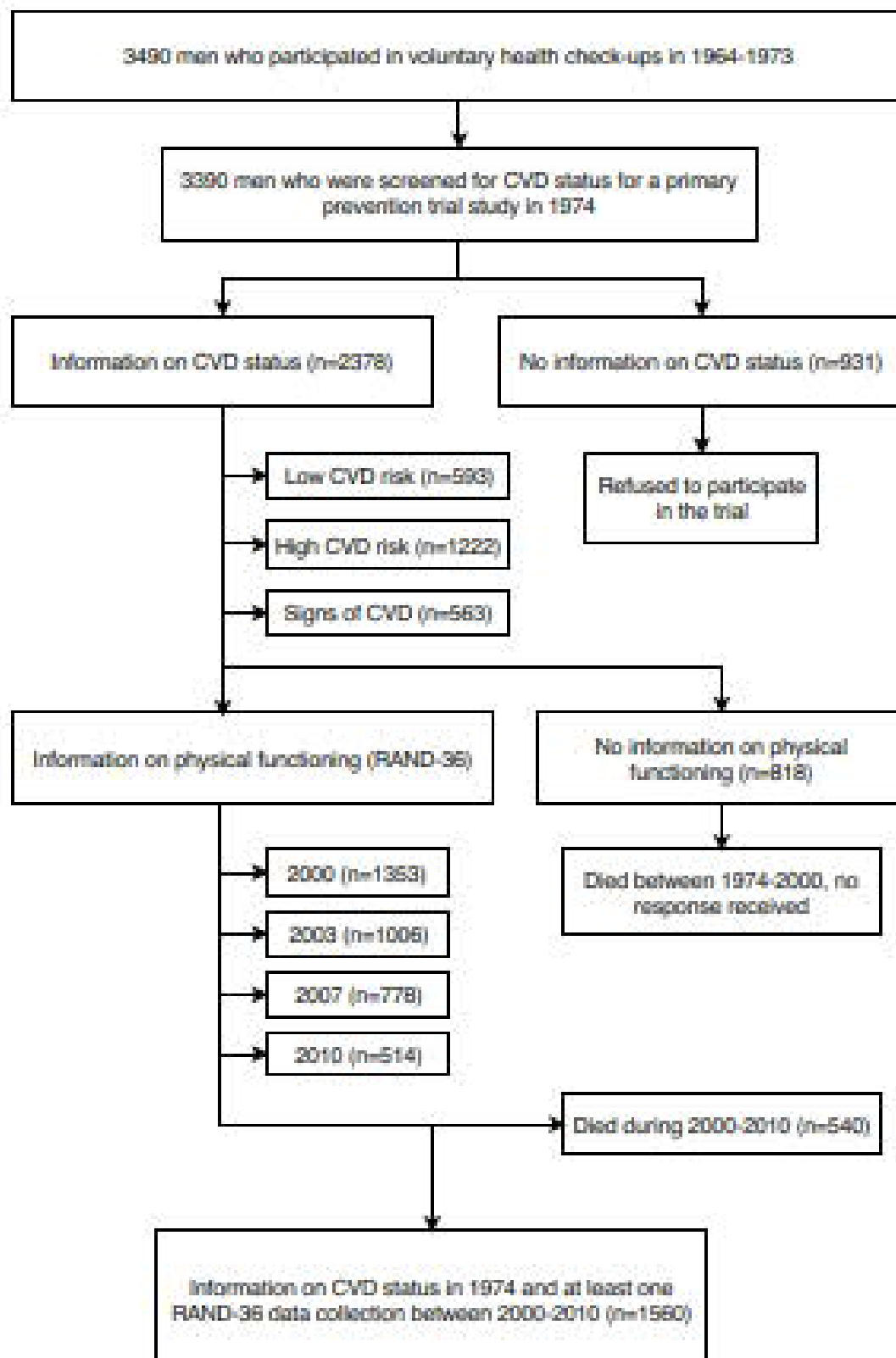


Figure 2.

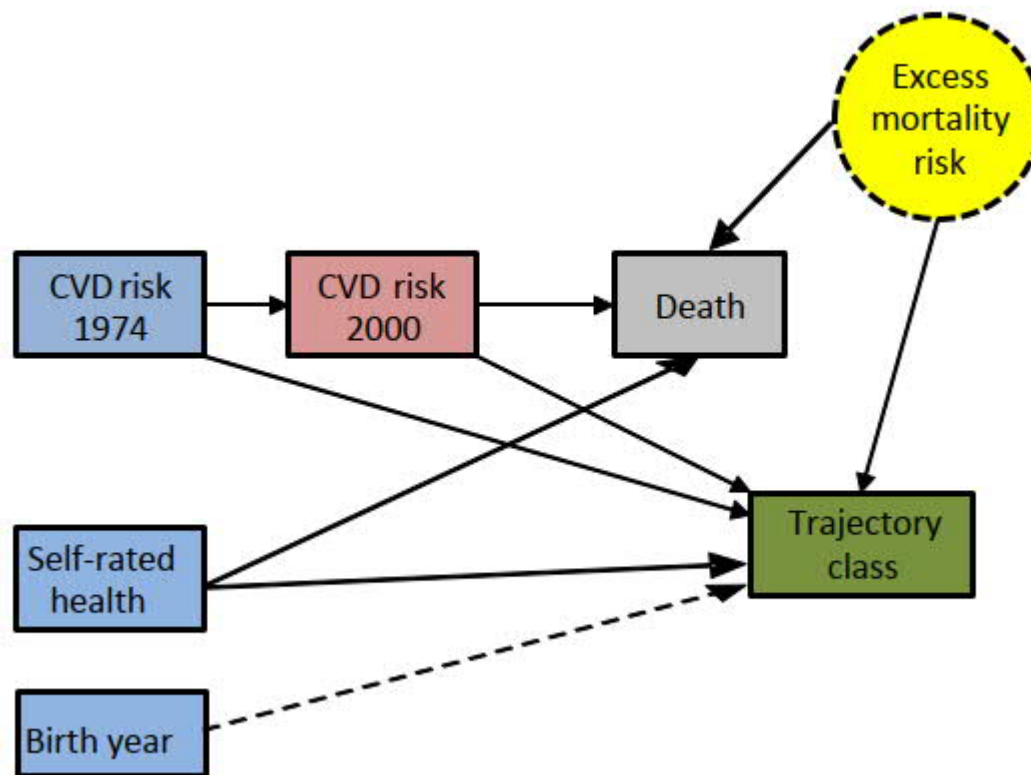
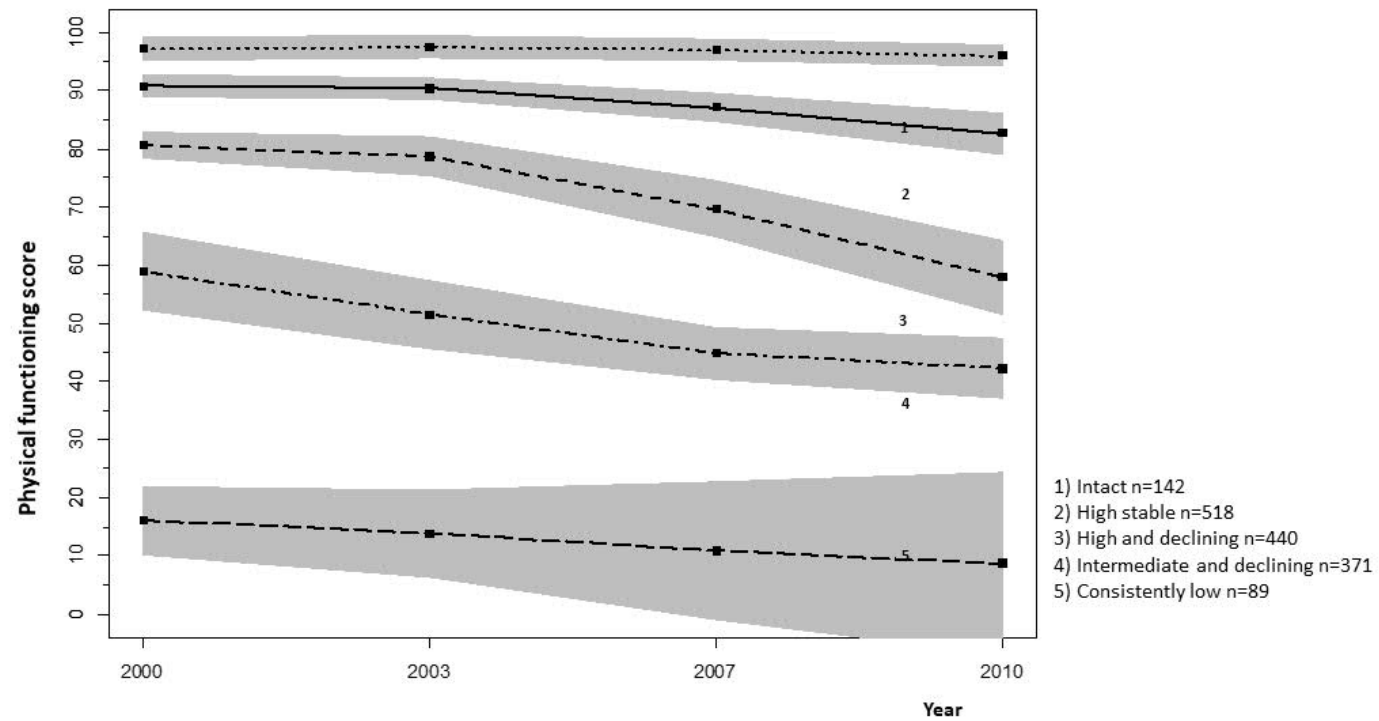


Figure 3



Supplementary Table S1. Model Fit Statistics, Group Sizes and Average Latent Class Probabilities for Most Likely Class Membership.

Classes	LL	Scaling	Free parameters	Information criteria				Group size (Average latent class probability for most likely latent class membership)					
				AIC	BIC	aBIC	Entropy	n ₁	n ₂	n ₃	n ₄	n ₅	n ₆
1	-21939	1.88	13	43904	43977	43935	1.000	1991 (1.00)					
2	-20815	1.26	27	41684	41835	41749	0.742	960 (0.95)	1031 (0.91)				
3 ^b	-20597	1.49	38	41270	41483	41362	0.712	742 (0.93)	818 (0.84)	431 (0.81)			
4 ^c	-20495	1.31	49	41087	41361	41206	0.691	610 (0.78)	198 (0.80)	517 (0.92)	666 (0.78)		
5 ^d	-20453	1.24	54	41009	41312	41140	0.712	556 (0.78)	191 (0.79)	461 (0.84)	631 (0.78)	152 (0.88)	
6 ^e	-20422	1.18	65	40973	41337	41131	0.658	535 (0.73)	189 (0.78)	139 (0.66)	619 (0.79)	377 (0.66)	132 (0.79)

Note. LL = loglikelihood, scaling = Robust maximum likelihood scaling factor, AIC = Akaike information criterion, BIC = Bayesian information criterion, aBIC = sample size adjusted Bayesian information criterion.

^bParameter restrictions in class 3: $\text{var}(Q)=0$, $\text{cov}(I,Q)=0$, $\text{cov}(S,Q)=0$.

^cParameter restrictions in class 2: $\text{var}(Q)=0$, $\text{cov}(I,Q)=0$, $\text{cov}(S,Q)=0$, and in class 3: $\text{var}(Q)=0$, $\text{cov}(I,Q)=0$, $\text{cov}(S,Q)=0$.

^dParameter restrictions in class 2: $\text{var}(Q)=0$, $\text{cov}(I,Q)=0$, $\text{cov}(S,Q)=0$, and in class 3: $\text{var}(I) = 0$, $\text{var}(S)$, $\text{var}(Q)=0$, $\text{cov}(I,Q)=0$, $\text{cov}(I,S) = 0$, $\text{cov}(S,Q)=0$, and in class 4: $\text{intercept}(Q)=0$, $\text{var}(I) = 0$, $\text{var}(Q)=0$, $\text{cov}(I,Q)=0$, $\text{cov}(I,S) = 0$, $\text{cov}(S,Q)=0$.

^eParameter restrictions in class

Supplementary Figure S1

